TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35.U.S.C. 371

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U S APPLICATION NO 09/719662

INTERNATIONAL APPLICATION NO	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/AU99/00735	08 SEPTEMBER 1999	11 SEPTEMBER 1998

TITLE OF INVENTION
MOUSSE COMPOSITION

APPLICANT(S) FOR DO/EO/US
Albert Zorko Abram

Applicant herewith submits to the United States Designated /Elected Office (DO/EO/US) the following items and other information:

1. [x] This is a FIRST submission of items concerning a filing under 35 U.S.C. 371.
2. [ ] This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371.
3. [x] This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(I).
4. [ ] A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. [ ] A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. [ ] is transmitted herewith (required only if not transmitted by the International Bureau).
   b. [ ] has been transmitted by the International Bureau.
   c. [ ] is not required, as the application was filed in the United States Receiving Office (RO/US).
6. [ ] A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. [ ] Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. [ ] are transmitted herewith (required only if not transmitted by the International Bureau).
   b. [ ] have been transmitted by the International Bureau
   c. [ ] have not been made; however, the time limit for making such amendments has NOT expired.
   d. [ ] have not been made and will not be made.
8. [ ] A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. [ ] An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. [ ] A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern other document(s) or information included:

11. [ ] An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. [ ] An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. [x] A FIRST preliminary amendment.
    [ ] A SECOND or SUBSEQUENT preliminary amendment.
14. [ ] A substitute specification.
15. [ ] A change of power of attorney and/or address letter.
16. [x] Other items or information:

International Publication WO 00/15193 (incl. 12 pages spec, 3 pages claims, 4 sheets of drawings)
International Search Report
International Preliminary Examination
PCT Request
PCT Demand

INTERNATIONAL APPLICATION NO PCT/AU99/00775 09/719662	INTERNATIONAL FILING DATE 08 SEPTEMBER 1999	PRIORITY DATE CLAIMED 11 SEPTEMBER 1998

17. [X] The following fees are submitted:

Basic National Fee (37 CFR 1.492(a)(1)-(5):

Neither international preliminary examination fee (37 CFR 1.482)

Nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO (1.492(a)(3)) $1,000.00

International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO (1.492(a)(5) $860.00

International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO(1.492(a)(2)) $710.00

International preliminary examination fee paid to USPTO (37 CFR 1.482) but all claims did not satisfy provisions of PCT Article 33(1)-(4) (1.492(a)(1)) $690.00

International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4) ..... $ 100.00

CALCULATIONS PTO USE ONLY

ENTER APPROPRIATE BASIC FEE AMOUNT =	$1,000	
Surcharge of $130.00 for furnishing the oath or declaration later than [ ] **20** [ ] **30** months from the earliest claimed priority date (37 C.F.R. 1.492(e)).	$	

Claims	**Number Filed**	**Number Extra**	**Rate**	$	
Total Claims	18 -20=		X $ 18.00	$	
Independent Claims	2 -3=		X $ 80.00	$	
Multiple dependent claim(s) (if applicable)			+ $270.00	$	
TOTAL OF ABOVE CALCULATIONS =				$1,000.00	
Reduction by ½ for filing by small entity, if applicable. Verified Small Entity statement must also be filed. (Note 37 CFR 1.9, 1.27, 1.28).				$ 500.00	
SUBTOTAL =				$ 500.00	
Processing fee of $130.00 for furnishing the English translation later than [ ] **20** [ ] **30** months from the earliest claimed priority date (37 CFR 1.492(f)).			+	$	
TOTAL NATIONAL FEE =				$ 500.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). $40.00 per property			+	$	
TOTAL FEES ENCLOSED =				$ 500.00	
				Amt. refunded	$
				charged	$

a. [X] A check in the amount of $ 500.00 to cover the above fees is enclosed.

b. [ ] Please charge our Deposit Account No. 02-4377 in amount of $___ to cover the above fees. A copy of this sheet is enclosed.

c. [X] The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 02-4377. A copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

BAKER BOTTS L.L.P.
30 Rockefeller Plaza
New York, New York 10112-4498

Signature RONALD B. HILDRETH

December 15, 2000
Date

19, 498
Registration No.

VERIFIED STATEMENT CLAIMING SMALL ENTITY STATUS (37 CFR 1.9(f) & 1.27(b)) - SMALL BUSINESS CONCERN

Applicant or Patentee: Soltec Research Pty Ltd

Serial or Patent No: _____

Filed or Issued: _____

Title: Mousse Composition

I hereby declare that I am

☐ the owner of the small business concern identified below;
☒ an official of the small business concern empowered to act on behalf of the concern identified below

NAME OF SMALL BUSINESS CONCERN Soltec Research Pty Ltd

ADDRESS OF SMALL BUSINESS CONCERN 8 Macro Court, Rowville, Victoria 3178, Australia

I hereby declare that the above identified small business concern qualifies as a small business concern as defined in 13 CFR 121.12, and reproduced in 37 CFR 1.9(d), for the purposes of paying reduced fees to the United States Patent and Trademark Office, in that the number of employees of the concern, including those of its affiliates, does not exceed 500 persons. For purposes of this statement, (1) the number of employees of the business concern is the average over the previous fiscal year of the concern of the persons employed on a full-time, part-time or temporary basis during each of the pay periods of the fiscal year, and (2) concerns are affiliates of each other when either, directly or indirectly, one concern controls or has the power to control the other, or a third party or parties controls or has the power to control both.

I hereby declare that rights under contract or law have been conveyed to and remain with the small business concern identified above with regard to the invention described in:

☒ the specification filed herewith with title as listed above
☐ the application identified above
☐ the patent identified above

If the rights held by the above identified small business concern are not exclusive, each individual, concern or organisation having rights in the invention must file separate verified statements averring to their status as small entities, and no rights to the invention are held by any person, other than the inventor, who would not qualify as an independent inventor under 37 CFR 1.9(c) if that person made the invention, or by any concern which would not qualify as a small business concern under 37 CFR 1.9(d), or a non profit organisation under 37 CFR 1.9(e).

Each person, concern or organisation having any rights in the invention is listed below:

☒ no such person, or organisation exists
☐ each such person, concern or organisation is listed below.

Separate verified statements are required from each named person, concern or organisation having rights to the invention averring to their status as small entities (37 CFR 1.27).

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlements to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate. (37 CFR 1.28(b)).

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that wilful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such wilful false statements may jeopardise the validity of the application, any patent issuing therein, or any patent to which this verified statement is directed.

NAME OF PERSON SIGNING Ross A. MACDONALD

TITLE OF PERSON IF OTHER THAN OWNER MANAGING DIRECTOR

ADDRESS OF PERSON SIGNING 35 MELVILLE ST. HAWTHORN, VIC. AUSTRALIA

SIGNATURE _____ DATE 19 December 2000

A33760 - 062635.0130

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Albert Zorko Abram

Serial No. : To be Assigned

Filed : To be Assigned

For : MOUSSE COMPOSITION

PRELIMINARY AMENDMENT

Assistant Commissioner of Patents

Washington, D.C. 20231

Sir:

Preliminary to the examination of the above-identified application, please make the following amendment to the claims:

In the Claims:

Cancel Claim 19.

REMARKS

Claim 19 has been cancelled since it does not conform to U.S. practice.

Respectfully submitted,

Ronald B. Hildreth
Patent Office Reg. No. 19,498

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MOUSSE COMPOSITION

The present invention provides a composition for the topical administration of pharmaceutical active ingredients.

Various aerosol and non-aerosol quick breaking and slow breaking foams for the topical delivery of pharmaceutical active ingredients are known in the prior art. In particular, the foam composition is an aqueous emulsion system. The foam composition upon actuation produces a stabilised, homogeneous, expandable foam which breaks easily with shear. A composition of this type is often referred to as an aerosol foam or "mousse".

It is known to use mousse compositions to topically deliver pharmaceutical active ingredients. An example of such a composition is in Australian patent application 80257/87 which discloses a mousse composition for the topical delivery of the pharmaceutically active ingredient, minoxidil. However the efficiency of such systems to deliver pharmaceutically active ingredients is limited.

Moreover, the majority of topical lotions and creams known or suggested in the prior art for delivering pharmaceutically active ingredients contain large amounts of petrolatum or some other occlusive agent to act as a barrier over the skin. This barrier reduces the evaporation of moisture from the skin which leads to increased moisture in the stratum corneum and in the epidermis and enhances the topical delivery of the pharmaceutical active ingredients.

However, in practice it would not be desirable to include such large amounts of an occlusive agent in a mousse formulation because when dispensed the mousse formulation would be a less stable foam, and upon application, the occlusive agent would leave a greasy, sticky lather on the skin which would not be considered acceptable to the consumer.

In prior art United States patents 5,002,680 and 4,981,677, there is disclosed mousse compositions that contain an occlusive agent such as petrolatum. These compositions are directed towards cosmetic purposes, and

provide no disclosure on their suitability or otherwise to enhance the topical delivery of pharmaceutical active ingredients. Further, in respect of United States Patent 4,981,677 the formulation includes a starch component. It is accordingly not apparent that an occlusive layer would be formed.

Accordingly, it would be a significant advance in the art if a mousse composition could be provided that enhanced the topical delivery of the pharmaceutical active ingredient while preferably still providing a pharmaceutically elegant and consumer acceptable composition.

In a first aspect of the present invention there is provided a pharmaceutical aerosol foam composition including an effective amount of

a pharmaceutically active ingredient

an occlusive agent

an aqueous solvent; and

an organic cosolvent;

the pharmaceutically active ingredient being insoluble in both water and the occlusive agent;

the occlusive agent being present in an amount sufficient to form an occlusive layer on the skin, in use.

The present invention is predicated on the surprising discovery that a mousse formulation with a relatively low amount of an occlusive agent is still able to reduce trans epidermal water loss and hence in theory increase skin permeability to effect greater drug skin penetration while remaining an elegant and consumer acceptable composition.

The water-insoluble pharmaceutically active ingredient may be any suitable type. An analgesic such as capsaicin or piroxicam, antifungal such as clotrimazole or miconazole nitrate, antibacterial such as nitrofurazone or gramcidin, anaesthetic such as benzocaine or lidocaine, antiviral such as aciclovir or penciclovir, antipruritic such as crotamiton or phenol, antihistamine such as chlorpheniramine or triprolidine, xanthine such as caffeine, sex hormone such as oestradiol or testosterone, anti-inflammatory agent or corticosteroid may be used.

A corticosteroid is preferred. The corticosteroids may be selected from one or more of the group consisting of, betamethasone valerate and clobetasol propionate.

Clobetasol propionate is preferred.

The pharmaceutically active ingredient may be present in any effective amounts. The pharmaceutically active ingredient may be present in amounts of approximately 0.005% by weight to approximately 10% by weight, preferably approximately 0.05% to approximately 1% by weight, based on the total weight of the pharmaceutical aerosol foam composition.

The aerosol foam base can be made using compositions that are well known in the art.

The pharmaceutical aerosol foam composition may further include an effective amount of an aerosol propellant. The aerosol propellant used in the mousse composition may be any suitable gas, such as a hydrocarbon, e.g. propane, butane, CFCs, HFCs, nitrogen or air. In a preferred embodiment the aerosol propellant is a hydrocarbon. Where the aerosol propellant is a hydrocarbon it may be present in an amount of from approximately 2.5% to 20% by weight, preferably 2.5% to 7.5% by weight, based on the total weight of the pharmaceutical mousse composition. The propellant may be introduced into the mousse composition at the time of filling utilising for example a standard aerosol dispenser, e.g. a spray can arrangement.

The occlusive agent utilised in the pharmaceutical composition according to the present invention may be any excipient or combination thereof that provides an occlusive layer or hydration barrier to the skin. An occlusive layer or hydration barrier is a layer or barrier sufficient to result in reduction in trans epidermal water loss, which results in skin hydration. Suitable occlusive agents may be selected from one or more of the group consisting of mineral oils and greases, long chain acids, animal fats and greases, vegetable fats and greases, water insoluble polymers and the like. In a preferred embodiment the occlusive agent is

petrolatum.

The occlusive agent is present in an amount sufficient to permit the formation of an occlusive layer or hydration barrier on the skin of the patient. Surprisingly applicants have discovered it is possible to form such an occlusive layer with a relatively low amount of occlusive agent. For example the amount of occlusive agent in the mousse composition may be up to approximately 55%, preferably approximately 40% or less by weight based on the total weight of the composition. In a preferred embodiment of the invention the amount of occlusive agent in the mousse composition may be up to approximately 50%, more preferably from approximately 20 to 50% by weight.

The pharmaceutical mousse composition may further include an effective amount of an emulsifier and/or surfactant.

The emulsifier or surfactant may be selected from one or more of the group consisting of non-ionic, anionic and cationic surfactants, e.g. fatty alcohols, fatty acids and fatty acid salts thereof.

Suitable emulsifiers or surfactants include pharmaceutically acceptable, non-toxic, non-ionic, anionic and cationic surfactants. Examples of suitable non-ionic surfactants include glycerol fatty acid esters such as glycerol monostearate, glycol fatty acid esters such as propylene glycol monostearate, polyhydric alcohol fatty acid esters such as polyethylene glycol (400) monooleate, polyoxyethylene fatty acid esters such as polyoxyethylene (40) stearate, polyoxyethylene fatty alcohol ethers such as polyoxyethylene (20) stearyl ether, polyoxyethylene sorbitan fatty acid esters such as polyoxyethylene sorbitan monostearate, sorbitan esters such as sorbitan monostearate, alkyl glycosides such as cetearyl glucoside, fatty acid ethanolamides and their derivatives such as the diethanolamide of stearic acid, and the like. Examples of suitable anionic surfactants are soaps including alkali soaps, such as sodium, potassium and ammonium salts of aliphatic carboxylic acids, usually fatty acids, such as sodium stearate. Organic amine soaps, also included, include organic amine salts of aliphatic carboxylic acids, usually fatty acids, such as triethanolamine stearate. Another class of

suitable soaps is the metallic soaps, salts of polyvalent metals and aliphatic carboxylic acids, usually fatty acids, such as aluminium stearate. Other classes of suitable anionic surfactants include sulfated fatty acid alcohols such as sodium lauryl sulfate, sulfated oils such as the sulfuric ester of ricinoleic acid disodium salt, and sulfonated compounds such as alkyl sulfonates including sodium cetane sulfonate, amide sulfonates such as sodium N-methyl-N-oleyl laurate, sulfonated dibasic acid esters such as sodium dioctyl sulfosuccinate, alkyl aryl sulfonates such as sodium dodecylbenzene sulfonate, alkyl naphthalene sulfonates such a sodium isopropyl naphthalene sulfonate, petroleum sulfonate such as aryl napthalene with alkyl substitutes. Examples of suitable cationic surfactants include amine salts such as octadecyl ammonium chloride, quarternary ammonium compounds such as benzalkonium chloride.

Surfactants which are a mixture of sorbitan monostearate and polysorbate 60 are preferred.

The emulsifier component may be present in any suitable stabilising amount. Preferably the emulsifier component may be in an amount where the ratio of emulsifier component to the occlusive agent, active pharmaceutical ingredient and cosolvent is about 1:5. The emulsifier component may be present in an amount of from approximately 1% to 15% by weight, preferably approximately 2.0% to 5.0% by weight, based on the total weight of the pharmaceutical mousse composition.

The aqueous solvent may be present in an amount of from approximately 25% to 95% by weight, preferably approximately 70% to 85% by weight, based on the total weight of the pharmaceutical mousse composition.

The composition further includes an organic cosolvent. The organic solvent may be an ester of a fatty acid for example a C12 – C15 alkyl benzoate, a medium to long chain alcohol, an aromatic and/or alkyl pyrollidinone, an aromatic and/or alkyl, and/or cyclic ketone, an aromatic and/or alkyl, and/or cyclic ether, substituted and/or unsubstituted single or multiple ring aromatic, straight chain and/or branched chain and/or cyclic alkane or silicone. The organic cosolvent may

be present in amounts of approximately 0.25% to 50% by weight, preferably 0.5 to 2% by weight, based on the total weight of the pharmaceutical mousse composition. Preferred organic cosolvents include C12 – C15 alkyl benzoates (FINSOLV TN) and caprylic/capric triglyceride (CRODAMOL GTCC).

The pharmaceutical mousse composition according to the present invention may also contain other non-essential ingredients. The composition may contain up to 10 weight percent of conventional pharmaceutical adjuvants. These adjuvants or additives include preservatives, stabilisers, antioxidants, pH adjusting agents, skin penetration enhancers, and viscosity modifying agents.

EXAMPLES

The present invention will now be more fully described with reference to the accompanying figures and examples. It should be understood that the description following is illustrative only and should not be taken in any way as restrictive on the generality of the foregoing description.

Figure 1 illustrates the effect of petrolatum content on in vitro epidermal penetration of clobetasol from topical mousse formulations 72 hours after application of 10mg/cm^2 of formulation.

Figure 2 illustrates the effect of petrolatum content on the rate of transepidermal water loss (TEWL) determined on the forearm of a healthy volunteer 30 and 120 minutes after topical application of 10mg/cm^2 of formulation.

Figure 3 illustrates relative decreases in the rate of transepidermal water loss (TEWL) observed on the forearm of a healthy volunteer with increasing concentrations of petrolatum in topically applied formulations.

Figure 4 illustrates the effect of application of a 50% petrolatum mousse formulation on the relative rate of TEWL on the forearm of healthy volunteers (mean±SD, n=6).

Example 1: Formulations

A series of 7 pharmaceutical formulations were prepared in accordance with the present invention. The composition of each formulation is given in Table 1.

Table 1

Ingredient	1	2	3	4	5	6	7
Petrolatum	10%	10%	20%	30%	30%	40%	50%
Clobetasol Propionate	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%
Caprylic/Capric Triglyceride	-	-	-	-	10%	-	-
Alkyl Benzoate	10%	10%	10%	10%	-	10%	10%
Cetearyl glucoside	2.5%	-	-	-	-	-	-
Sorbitan Stearate	-	1.63%	2.54%	3.44%	3.02%	4.35%	5.25%
Polysorbate 60	-	2.37%	3.46%	4.56%	4.98%	5.65%	6.75%
Water	72.25 %	70.95 %	58.95 %	46.95 %	46.95 %	34.95 %	22.95%
Preservatives	0.2%	-	-	-	-	-	-
Propellant	5%	5%	5%	5%	5%	5%	5%

Example 2: Effect of Petrolatum Concentration on the In-vitro Epidermal Penetration of Clobetasol from Topical Mousse Formulations

Aim

The aim of the study was to:

(1) determine the penetration of the steroid clobetasol into human epidermis following topical application of mousse formulations to which increasing concentrations of petrolatum had been included as a potential occlusive agent and penetration enhancer.

(2) To assess clobetasol penetration following application to intact epidermis and that which had been stripped 3 times with tape to model the impaired stratum corneum barrier function seen in the dermatological conditions for which the drug is used clinically.

Method

Preparation of epidermal membranes: Donated human female abdominal skin was separated by blunt dissection, to remove subcutaneous fat and extraneous tissue, and immersed in water at 60°C for 2 minutes to allow separation of the epidermal-dermal junction. Epidermal membranes were lifted from the dermis by gently rolling from one end with the fingers and stored on filter paper, stratum corneum uppermost, at -20°C until use.

Diffusion Studies Epidermal membranes were mounted, stratum corneum uppermost and facing the donor chamber, on filter paper between the two halves of standard horizontal glass Franz-type diffusion cells (area approx. 1.3cm^2). The bottom half of the diffusion cells was filled with approximately 3.5ml of receptor medium (either 20% ethanol in distilled water for intact epidermal membrane studies or Baxter 20% Intralipid® solution for stripped skin studies) and continuously stirred with small magnetic fleas. Assembled cells were semi-submerged in a water bath maintained at 35±0.1°C.

Mousse formulations containing 0.05% clobetasol with the inclusion of 0, 30 or 50% petrolatum were gently applied to the donor chamber with a round-ended plastic rod which was wiped around the skin surface such that the skin was covered by a total dose of approximately 10mg/cm^2. The weight of formulation applied was verified from the difference in weight of the application rod and small weigh boat from which the formulation had been applied before and after dosing.

Clobetasol was allowed to penetrate into the epidermis for 72hrs after which time the remaining formulation was removed from the skin surface by washing and a single tape strip was performed to ensure that minimal 'unpenetrated' material remained on the surface of the epidermis. All washes and

tape strips were retained for quantification of clobetasol concentration. The area of epidermis exposed to the formulation was then removed from the membrane using a stainless steel punch which was cleaned with methanol between samples to avoid any cross contamination of clobetasol. Epidermal, tape and wash samples were all assayed for clobetasol concentration by high performance liquid chromatography.

Results

Figure 1 shows the fraction of the applied amount of clobetasol that was found to have penetrated into the epidermal membranes during the study. It can be clearly seen that inclusion of petrolatum in the mousse formulations has increased the amount of clobetasol penetrating into the epidermis of both intact and stripped skin samples. The recovery of the applied amounts of clobetasol in the washes; tape strip and epidermis was greater than 75% in all cases.

Conclusion

Increasing concentrations of petrolatum in topical mousse formulations containing 0.05% clobetasol was able to increase the in-vitro human epidermal penetration of the steroid in both intact and stripped skin models.

Example 3a: The Effect of Petrolatum Concentration on the Occlusivity of Topical Mousse Formulations

Aim

The aim of the study was to determine whether increasing the concentration of petrolatum in topical mousse formulations could effectively occlude the underlying skin and thereby lead to increased local hydration which in turn is known to improve the percutaneous penetration of suitable drugs.

Method

Relative degrees of occlusion of the skin in humans can be effectively quantified by following changes in the normal rate of transepidermal water loss (TEWL) caused by procedures such as formulation application. In the present study a commercially available single probe TEWL meter (Tewameter, Courage and Khazaka, Cologne, Germany) was used to determine the rate of TEWL ($g/hr/m^2$) at a number of 2x2cm numbered test squares marked on the medial side of the forearm of a healthy volunteer. Baseline readings of TEWL were taken in triplicate at each test site prior to the application of mousse formulation at a dose of $10mg/cm^2$ containing 0, 10, 20, 30, 40 or 50% petrolatum. To ensure that the dose rate of $10mg/cm^2$ was maintained for each formulation, approximately 40mg of each mousse was weighed out onto a 2cm wide glass slide which was then used to wipe the mousse evenly across each one of the marked test squares before being reweighed to determine the total amount of mousse transferred onto the skin.

At 30 and 120 minutes following mousse application determinations of TEWL were repeated at each of the test sites. Relative changes in TEWL were then calculated by dividing the rate of TEWL following application by that taken from the same marked square at t=0.

Results

Figure 2 shows the actual rate of TEWL ($g/hr/m^2$) determined at each of the test sites prior to treatment and again at 30 and 120 minutes after mousse application. A decrease in the rate of TEWL was observed with increasing concentrations of petrolatum in the mousse formulations at both 30 and 120 minutes following application. Figure 2 clearly shows the relationship between the % of petrolatum content in each of the test mousses and the resultant relative change in the rate of TEWL determined at 30 and 120 minutes after formulation application.

Conclusion

Increasing the concentration of petrolatum in topical mousse formulations was able to decrease the normal rate of TEWL on the forearm of a healthy volunteer. The decreases in the rate TEWL observed effectively demonstrate that increasing the concentration of petrolatum in the product leads to an increase in the relative occlusivity of the topical mousse formulations tested .

Example 3b

Part 2

Aim

The aim of the second part of this study was to assess the degree of occlusivity afforded by the 50% petrolatum mousse formulation in a number of healthy volunteers.

Method

The effect of a 10mg/cm^2 dose of 50% mousse formulation on the normal rate of TEWL was determined on the forearm of 6 volunteers in a manner identical to that described above. The relative changes observed in the rate of TEWL at 30 and 120 min after application were then compared to an untreated control site measured at the same time on the tested forearm of each volunteer.

Results

Figure 4 shows the relative rates of TEWL determined at the 2 test sites on the forearms of the volunteers. Significant decreases in TEWL ($P<0.05$, ANOVA and Students t-test) were observed at both the 30 and 120 min post-treatment tests following application of the 50% petrolatum mousse formulation. No significant difference was observed in the rate of TEWL between the control sites over the 120 min test period ($P=0.19$, ANOVA).

Conclusion

Application of a mousse formulation containing 50% petrolatum at a dose of 10mg/cm^2 significantly occluded the skin as determined by decreases in the rate of TEWL observed on the forearms of 6 healthy volunteers.

Finally, it is to be understood that various alterations, modifications and/or additions may be made without departing from the spirit of the present invention as outlined herein.

CLAIMS

1 A pharmaceutical aerosol foam composition including an effective amount of

a pharmaceutically active ingredient

an occlusive agent;

an aqueous solvent; and

an organic cosolvent

the pharmaceutically active ingredient being insoluble in both water and the occlusive agent;

the occlusive agent being present in an amount sufficient to form an occlusive layer on the skin, in use.

2. A pharmaceutical aerosol foam composition according to Claim 1, wherein the water insoluble pharmaceutically active ingredient is selected from one or more of the group consisting of an analgesic, anti-inflammatory agent, antifungal, antibacterial, anaesthetic, xanthine, sex hormone, antiviral, antipruritic, antihistamine or corticosteroid.

3. A pharmaceutical aerosol foam composition according to Claim 2, wherein the pharmaceutically active ingredient is a corticosteroid selected from one or more of the group consisting of, betamethasone valerate, and clobetasol propionate.

4. A pharmaceutical aerosol foam composition according to Claim 1, wherein the pharmaceutically active ingredient is present in amounts of from approximately 0.005% by weight to approximately 10% by weight, based on the total weight of the pharmaceutical mousse composition.

5. A pharmaceutical aerosol foam composition according to Claim 1, wherein the occlusive agent is selected from one or more of the group consisting of mineral oils and greases, long chain acids, animal fats and greases, vegetable fats and greases and water insoluble polymers.

6. A pharmaceutical aerosol foam composition according to Claim 5, wherein the occlusive agent includes petrolatum.

7. A pharmaceutical aerosol foam composition according to Claim 1, wherein the occlusive agent is present in an amount of approximately 55% by weight or less, based on the total weight of the composition.

8. A pharmaceutical aerosol foam composition according to Claim 7, wherein the occlusive agent is present in an amount of approximately 10 to 50% by weight, based on the total weight of the composition.

9. A pharmaceutical aerosol foam composition according to Claim 1, further including an effective amount of an emulsifier and/or surfactant.

10. A pharmaceutical aerosol foam composition according to Claim 9, wherein the emulsifier or surfactant is selected from any one or more of the group consisting of non-ionic, cationic or anionic surfactants, fatty alcohols, fatty acids and fatty acid salts thereof.

11. A pharmaceutical aerosol foam composition according to Claim 10, wherein the emulsifier includes a mixture of sorbitan monostearate and polysorbate 60.

12. A pharmaceutical aerosol foam composition according to Claim 9, wherein the surfactant component is present in an amount of from approximately 1 to 15% by weight, based on the total weight of the composition.

13. A pharmaceutical aerosol foam composition according to Claim 1, wherein the aqueous solvent is present in an amount of from approximately 25 to 95% by weight, based on the total weight of the composition.

14. A pharmaceutical aerosol foam composition according to Claim 13, wherein the organic cosolvent is present in an amount of from approximately 0.25% by weight to 50% by weight, based on the total weight of the composition.

15. A pharmaceutical aerosol foam composition according to claim 14 wherein the organic cosolvent is an alkyl benzoate.

16. A pharmaceutical aerosol foam composition according to Claim 1, further including an effective amount of an aerosol propellant.

17. A pharmaceutical aerosol foam composition according to Claim 16, wherein the aerosol propellant is a hydrocarbon and is present in an amount of from approximately 2.5 to 20% by weight, based on the total weight of the composition.

18. A pharmaceutical aerosol dispenser including a pharmaceutical aerosol foam composition including

an effective amount of

a pharmaceutically active ingredient

an occlusive agent;

an aqueous solvent;

an organic cosolvent.

the pharmaceutically active ingredient being insoluble in both water and the occlusive agent;

the occlusive agent being present in an amount sufficient to form an occlusive layer on the skin, in use.

19. A pharmaceutical aerosol foam composition substantially as hereinbefore described with reference to any one of the examples.

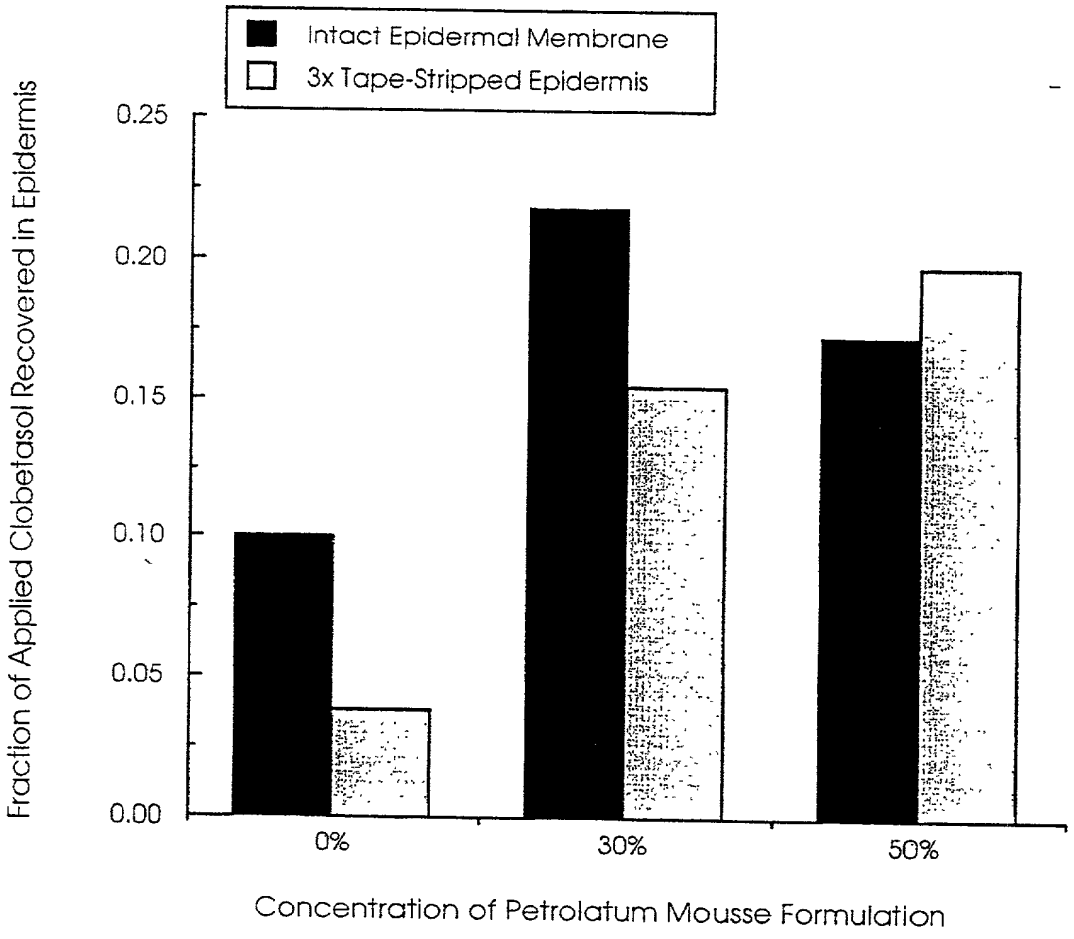
Intact Epidermal Membrane
3x Tape-Stripped Epidermis
Fraction of Applied Clobetasol Recovered in Epidermis
0.25
0.20
0.15
0.10
0.05
0.00
0%
30%
50%
Concentration of Petrolatum Mousse Formulation

Figure 1

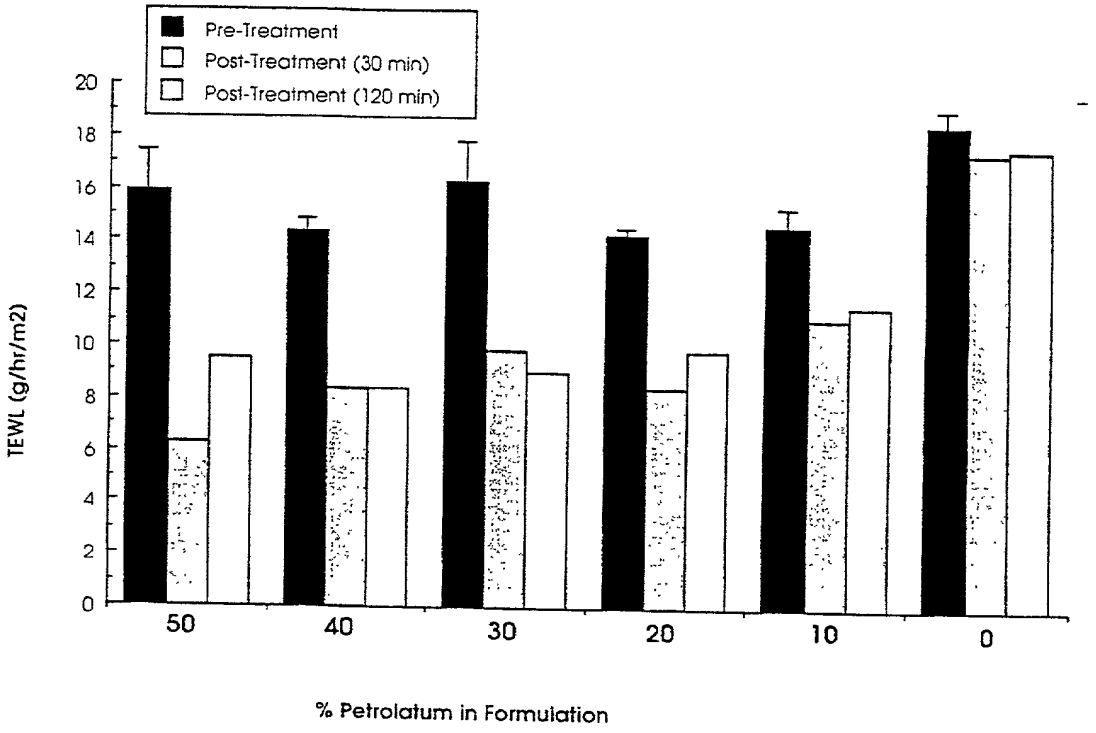

Figure 2

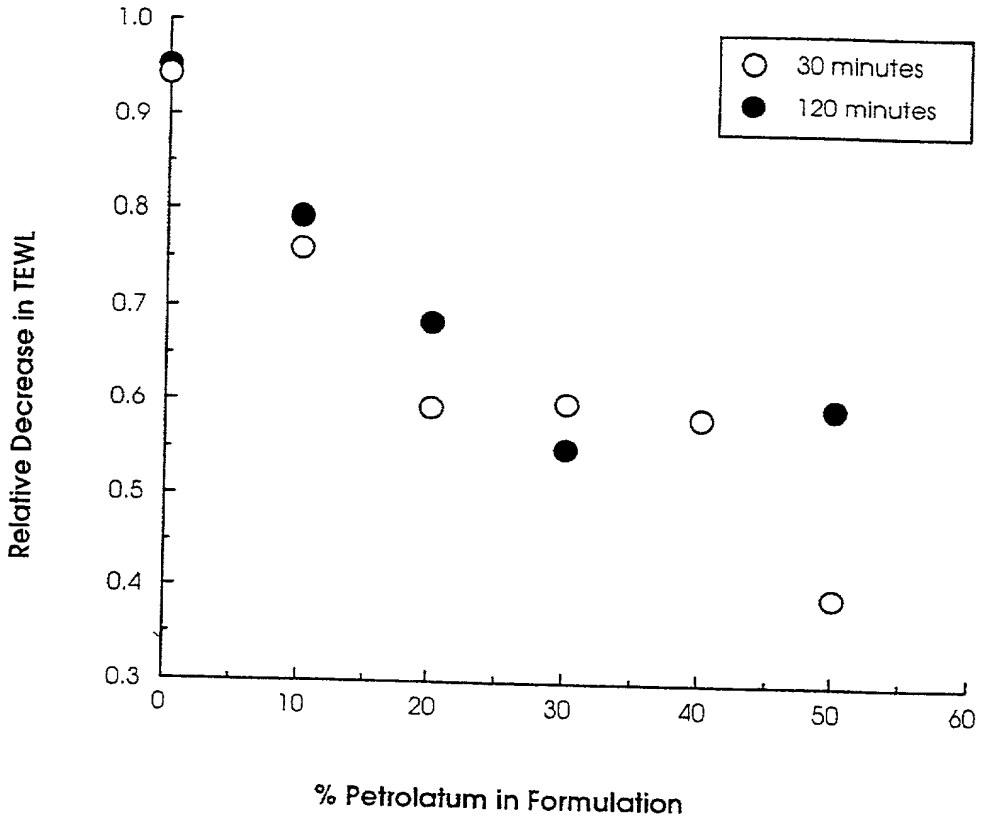

Figure 3

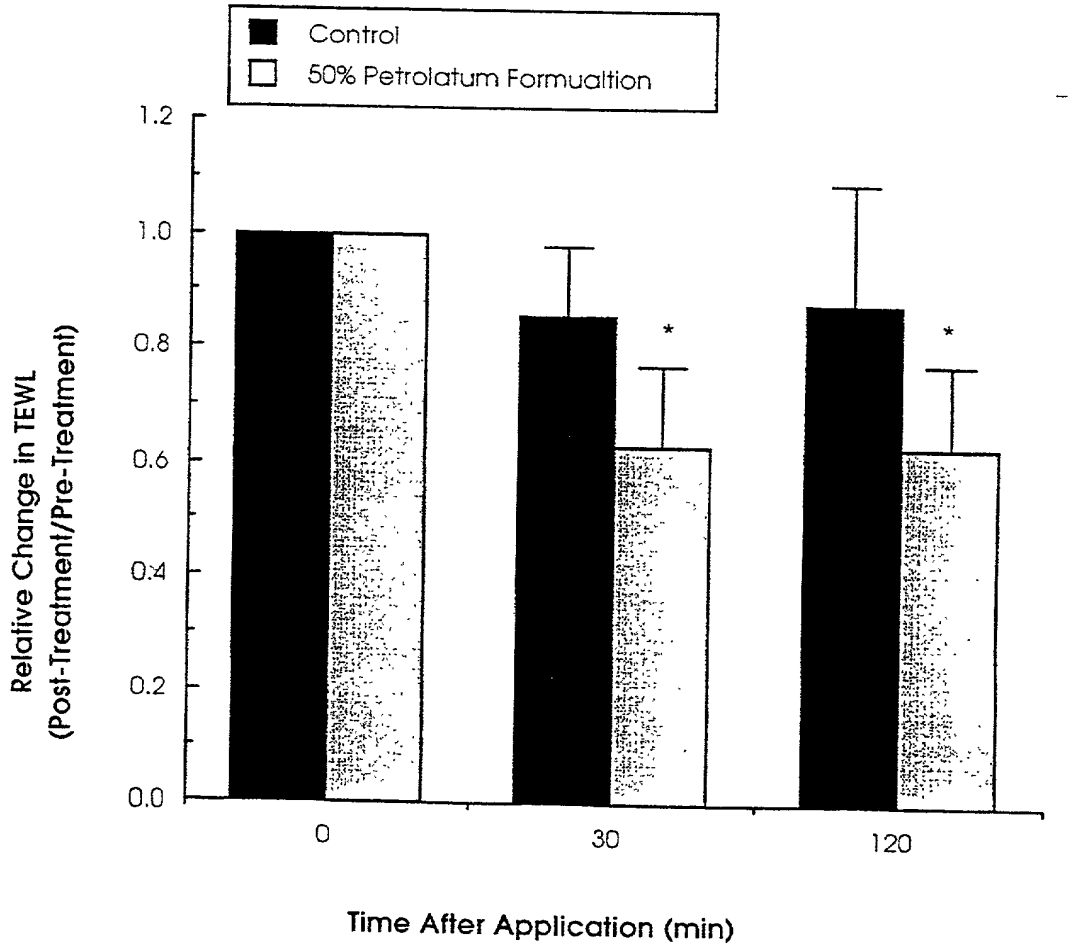
Control
50% Petrolatum Formualtion
Relative Change in TEWL
(Post-Treatment/Pre-Treatment)
1.2
1.0
0.8
0.6
0.4
0.2
0.0
*
*
0
30
120
Time After Application (min)

Figure 4

COMBINED DECLARATION AND POWER OF ATTORNEY

(Original, Design, National Stage of PCT, Divisional, Continuation or C-I-P Application)

s a below named inventor, I hereby declare that:
ly residence, post office address and citizenship are as stated below next to my name; I believe I am the original, rst and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are sted below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

his declaration is of the following type:

- [] original
- [] design
- [X] national stage of PCT.
- [] divisional
- [] continuation
- [] continuation-in-part (C-I-P)

e specification of which: *(complete (a), (b), or (c))*

) [X] is attached hereto.
) [ ] was filed on as Application Serial No. and was amended on *(if applicable)*.
) [ ] was described and claimed in PCT International Application No. filed on and was amended on *(if plicable)*.

Acknowledgement of Review of Papers and Duty of Candor

I hereby state that I have reviewed and understand the contents of the above identified specification, :luding the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the patentability of the subject matter imed in this application in accordance with Title 37, Code of Federal Regulations § 1.56.

[ ] In compliance with this duty there is attached an information disclosure statement. 37 CFR 1.98.

Priority Claim

I hereby claim foreign priority benefits under Title 35, United States Code, § 119(a)-(d) of any foreign)lication(s) for patent or inventor's certificate or of any PCT International Application(s) designating at least one intry other than the United States of America listed below and have also identified below any foreign)lication(s) for patent or inventor's certificate or any PCT International Application(s) designating at least one intry other than the United States of America filed by me on the same subject matter having a filing date before t of the application on which priority is claimed

(complete (d) or (e))

[ ] no such applications have been filed.
[X] such applications have been filed as follows:

PRIOR FOREIGN/PCT APPLICATION(S) FILED WITHIN 12 MONTHS (6 MONTHS FOR DESIGN) PRIOR TO SAID APPLICATION			
COUNTRY APPLICATION NO.	DATE OF FILING (day, month, year)	DATE OF ISSUE (day, month, year)	PRIORITY CLAIMED UNDER 35 USC 119
			[ ] YES NO [ ]
			[ ] YES NO [ ]
			[ ] YES NO [ ]
ALL FOREIGN APPLICATION[S], IF ANY, FILED MORE THAN 12 MONTHS (6 MONTHS FOR DESIGN) PRIOR TO SAID APPLICATION			
AUSTRALIA PP 5831	11/09/1998		[X] YES NO [ ]
AUSTRALIA PCT/AU99/00735	08/09/1999		[X] YES NO [ ]
			[ ] YES NO [ ]

Claim for Benefit of Prior U.S. Provisional Application(s)

I hereby claim the benefit under Title 35, United States Code, § 119(e) of any United States provisional application(s) listed below:

Provisional Application Number	Filing Date

Claim for Benefit of Earlier U.S./PCT Application(s) under 35 U.S.C. 120

(complete this part only if this is a divisional, continuation or C-I-P application)

I hereby claim the benefit under Title 35, United States Code, § 120 of any United States application(s) or PCT international application(s) designating the United States of America that is/are listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior application(s) in the manner provided by the first paragraph of Title 35, United States Code § 112, I acknowledge the duty to disclose information as defined in Title 37, Code of Federal Regulations, § 1.56 which occurred between the filing date of the prior application(s) and the national or PCT international filing date of this application:

lication Serial No.)	(Filing Date)	(Status) (patented, pending, abandoned)
lication Serial No.)	(Filing Date)	(Status) (patented, pending, abandoned)

Power of Attorney

As named inventor, I hereby appoint Dana M. Raymond, Reg. No. 18,540, Frederick C. Carver, Reg. No. 17,021; Francis J. Hone. Reg. No. 18,662; Joseph D. Garon, Reg. No. 20,420; Arthur S. Tenser, Reg. No. 18,839; Ronald B. Hildreth, Reg. No. 19,498; Thomas R. Boitt, Jr., Reg. No. 22,075; Robert Neuner, Reg. No. 24,316; Richard G. Berkley, Reg. No. 25,465; Richard S. Clark, Reg. No. 26,154; Kelley B. Geist, Reg. No. 27,551; James J. Maune, Reg. No. 26,946; John D. Murnane, Reg. No. 29,836, Henry Tang, Reg. No. 29,705, Robert C. Scheinfeld, Reg. No. 31,300, John A. Fogarty, Jr., Reg. No. 22,348, Louis S. Sorell, Reg. No. 32,439 and Rochelle K. Seide Reg. No. 32,300 of the firm of BAKER & BOTTS, L.L.P., with offices at 30 Rockefeller Plaza, New York, New York 10112, as attorney s to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith

SEND CORRESPONDENCE TO:	DIRECT TELEPHONE CALLS TO:
BAKER & BOTTS, L.L.P. 30 ROCKEFELLER PLAZA, NEW YORK, N.Y. 10112 CUSTOMER NUMBER: 21003	BAKER & BOTTS, L.L.P. (212) 705-5000

I hereby declare that all statements made herein of my own knowledge are true and that all statements made information and belief are believed to be true; and further that these statements were made with the knowledge willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section

1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

FULL NAME OF SOLE OR FIRST INVENTOR	LAST NAME ABRAM	FIRST NAME ALBERT	MIDDLE NAME ZORKO	
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POST OFFICE ADDRESS	POST OFFICE ADDRESS 3 ABBEY COURT	CITY WANTIRNA	STATE or COUNTRY VICTORIA	ZIP CODE 3152
DATE 1/12/00	SIGNATURE OF INVENTOR			
FULL NAME OF SECOND JOINT INVENTOR, IF ANY	LAST NAME	FIRST NAME	MIDDLE NAME	
RESIDENCE & CITIZENSHIP	CITY	STATE or FOREIGN COUNTRY	COUNTRY OF CITIZENSHIP	
POST OFFICE ADDRESS	POST OFFICE ADDRESS	CITY	STATE or COUNTRY	ZIP CODE
DATE	SIGNATURE OF INVENTOR			
FULL NAME OF THIRD JOINT INVENTOR, IF ANY	LAST NAME	FIRST NAME	MIDDLE NAME	
RESIDENCE & CITIZENSHIP	CITY	STATE or FOREIGN COUNTRY	COUNTRY OF CITIZENSHIP	
POST OFFICE ADDRESS	POST OFFICE ADDRESS	CITY	STATE or COUNTRY	ZIP CODE
DATE	SIGNATURE OF INVENTOR			
FULL NAME OF FOURTH JOINT INVENTOR, IF ANY	LAST NAME	FIRST NAME	MIDDLE NAME	
RESIDENCE & CITIZENSHIP	CITY	STATE or FOREIGN COUNTRY	COUNTRY OF CITIZENSHIP	
POST OFFICE ADDRESS	POST OFFICE ADDRESS	CITY	STATE or COUNTRY	ZIP CODE
DATE	SIGNATURE OF INVENTOR			
FULL NAME OF FIFTH JOINT INVENTOR, IF ANY	LAST NAME	FIRST NAME	MIDDLE NAME	
RESIDENCE & CITIZENSHIP	CITY	STATE or FOREIGN COUNTRY	COUNTRY OF CITIZENSHIP	
POST OFFICE ADDRESS	POST OFFICE ADDRESS	CITY	STATE or COUNTRY	ZIP CODE
DATE	SIGNATURE OF INVENTOR			
FULL NAME OF SIXTH JOINT INVENTOR, IF ANY	LAST NAME	FIRST NAME	MIDDLE NAME	
RESIDENCE & CITIZENSHIP	CITY	STATE or FOREIGN COUNTRY	COUNTRY OF CITIZENSHIP	
POST OFFICE ADDRESS	POST OFFICE ADDRESS	CITY	STATE or COUNTRY	ZIP CODE
DATE	SIGNATURE OF INVENTOR			